

### **REMARKS**

The present amendment is in response to the Advisory Action mailed April 9, 2009 and supplements the previous Amendment And Reply Under 37 CFR §1.116 dated March 9, 2009 in response to the Final Office Action mailed December 10, 2008. The present amendment has been made based on the claims filed in the Amendment dated March 9, 2009, which was entered as indicated by the Examiner in the Advisory Action. Applicants respectfully request the Examiner consider the present amendment and the following remarks as addressing the Examiner's comments made in the Advisory Action of April 9, 2009 and the remaining rejection set forth in the Final Office Action of December 10, 2008. A Request for Continued Examination is filed together with this paper.

After entry of this amendment, claims 1, 3, 7-9, 11, 14, 16-17, 19-20, 23 and 25 are pending. Claims 6, 15, 26 and 27 have been cancelled without prejudice or disclaimer. Claims 1, 7 and 14 have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. Further support for the amendment made to the claims is found in the specification at page 10, lines 27-33. No new matter has been added.

### **Claim Rejection – 35 U.S.C. § 103**

Claims 1-3, 6-9, 11, 14-17, 19, 20, 23 and 25-27 remain rejected under 35 U.S.C. § 103(a) as being obvious over Simmons *et al.* (hereinafter "Simmons") in view of Hückelhoven *et al.* (hereinafter "Hückelhoven"). The Examiner contends that the use of a tissue-specific promoter that is different from what was taught in the prior art would not render the claimed method unobvious. Specifically, the Examiner asserts that Simmons teaches methods of altering BI1 expression in transgenic plants using tissue-specific promoters, citing Example 7. The Examiner further asserts that Simmons teaches methods of inducing disease resistance by altering expression of the BI1 gene in tissues which are most accounting for the pathogen ingress using tissue-specific promoters, citing Example 11. The Examiner also alleges that Simmons teaches reducing the expression level of BI1 protein by using antisense BI1 construct containing tissue-specific promoter, citing Example 13. Advisory Action at page 2. Applicants respectfully disagree. However, to expedite prosecution, claim 1 has been amended without prejudice or disclaimer to specify that the expression of the at least one BI1 protein in the transgenic plant is under control of a mesophyll-specific promoter. Reconsideration and withdrawal of the rejection

is respectfully requested in light of the present claim amendment and further in view of the following reasons.

To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994). Additionally, it is noted that the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), indicated that the *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), factors still control an obviousness inquiry. Among other things, the “scope and content of the prior art” and the “differences between the prior art and the claims” must be considered.

The Examiner relies on two references, (1) Simmons, and (2) Hückelhoven, to support the finding of obviousness.

Simmons discloses BI genes from corn and soybean, and methods of using these sequences in generating transgenic plants and in improving disease and stress resistance. As the Examiner noted, Simmons teaches overexpressing BI gene with tissue-specific promoters such as root-, seed- or flower-specific promoter. Reading the reference as a whole, the tissue-specific promoter taught in Simmons refers only to promoters that direct gene expression in various plant parts or organs such as leaves, roots, fruits, seeds or flowers, but not a particular cell layer within a plant part or organ. As known to one skilled in the art, a plant part or organ may consist of various cell layers serving different functions. For instance, plant leaf consists of an epidermis that covers the upper and lower surfaces, an interior chlorenchyma called the mesophyll, and an arrangement of veins (the vascular tissue). However, none of the promoters taught in Simmons would specifically direct the expression of the BI1 protein in the leaf mesophyll of the transgenic plant while the expression in the epidermis remains essentially unchanged or reduced.

Hückelhoven teaches a nucleic acid encoding a BI1 protein that is 100% identical to SEQ ID NO: 2. While showing the gene expression profile in barley in response to *Blumeria graminis* f.sp. *hordei* (*Bgh*) inoculation, Hückelhoven does not teach or suggest transgenically expressing the disclosed gene with a tissue-specific promoter. Nor does Hückelhoven teach or suggest the use of a mesophyll-specific promoter to specifically express the BI1 gene in the leaf mesophyll, but not the epidermis.

It is thus apparent that the “differences between the prior art and the claims” primarily

lies on the use of a mesophyll-specific promoter to express a BI1 gene in a plant. The cited references, alone or in combination, do not teach or suggest the use of a mesophyll-specific promoter to express a BI1 gene in a plant so the expression of the BI1 protein would be increased in the leaf mesophyll of the transgenic plant while remaining essentially unchanged or reduced in the epidermis.

As amended, claim 1 recites that the expression of the at least one BI1 protein is under control of a mesophyll-specific promoter. Due to the specificity of the promoter used, the expression of the BI1 gene would be increased in the leaf mesophyll while the expression in the leaf epidermis in the same plant remains essentially unchanged or is reduced. As disclosed in the specification at page 4, lines 31-35, this particular expression pattern makes possible an efficient defense against plant pathogens such as necrotrophic pathogens without breaking any other existing resistance to other pathogens such as biotrophic pathogens. This is because the mesophyll-specific expression provides advantages in contributing resistance against fungi that attack preferably the mesophyll. Applicants submit that, at the time the present application was filed, it was not known in the art that different fungi attack plants *via* different routes: some fungi attack the plant *via* epidermis, while others attack the plant *via* the mesophyll. By specifically expressing a resistance gene in a particular cell layer, a better resistance to a pathogen attacking that cell layer could be achieved. Moreover, as mentioned above, the mesophyll is the interior cell layer below the epidermis. Because a person skilled in the art did not appreciate the different mechanisms by which fungi attack plants at the time of filing, one would naturally assume that the point of entry for the pathogen would be the epidermis and not the mesophyll. None of the cited references teaches or suggests the attacking mechanism *via* mesophyll. Without such teaching or suggestion, one skilled artisan would not have been motivated to use a mesophyll-specific promoter to express a BI1 gene in order to avoid breaking any other existing resistance to other pathogens.

Because the cited references, alone or in combination, do not teach or suggest the use of a mesophyll-specific promoter to express a BI1 gene, the combined teaching does not disclose or suggest all the limitations of the claimed method. Accordingly, a *prima facie* obviousness has not been established.

Moreover, as discussed in Applicants' response dated March 9, 2009, it is well

established that under 35 U.S.C. § 103 the Examiner must consider the subject matter sought to be patented as a whole. See MPEP § 2141.02. As part of the “subject matter as a whole” consideration, “a patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. *In re Spinnoble*, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969). Thus, where the inventor discovered a cause of problem and there was no teaching in the prior art which would suggest a solution for such a problem, the invention directing to solving that problem is nonobvious and thus patentable. *See id.*

As discussed above, neither Simmons nor Hüchelhoven teaches or suggests the pathogen’s attacking mechanism *via* mesophyll. Neither Simmons nor Hüchelhoven recognizes the problem where constitutive expression of a BII protein in a plant, while conferring resistance to necrotrophic fungi, breaks the mlo-mediated resistance to the obligate-biotrophic powdery mildew. As a result, neither Simmons nor Hüchelhoven recognizes the significant negative effect in the economical use of the methods taught therein in improving disease resistance in plants. By recognizing the cause of problem, Applicants provide in the present application a novel method in efficiently defending plant pathogens, preferably necrotrophic pathogens, without breaking any other existing resistance to other pathogens, such as biotrophic pathogens, by manipulating the expression level of the BII gene in different cell layers of leaves in a transgenic plant. Accordingly, it is respectfully submitted that the claimed subject matter, as amended, when considered as a whole, is nonobvious over the prior art and thus patentable.

For at least the above reasons and further in light of the present amendment, Applicants submit that Simmons and Hüchelhoven, alone or in combination, do not render the claimed subject matter as amended obvious. Reconsideration and withdrawal of the rejection is respectfully requested.

### **CONCLUSION**

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a Request for Continued Examination and a petition for two-month extension of time to and including May 10, 2009 with the required fee authorization.

No further fee is believed due. However, if any additional fee or credit is due, the Director is hereby authorized to charge or credit our Deposit Account No. 03-2775, under Order No. 12810-00137-US from which the undersigned is authorized to draw.

Respectfully submitted,

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